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# DEFECTIVE NEUTROPHIL CANDIDACIDAL ACTIVITY IN PATIENTS WITH RESISTANCE TO 1,25-DIHYDROXY-VITAMIN D<sub>3</sub> (1,25-D) WITH ALOPECIA. A. Etzioni, Y. Weissman, S. Pollack, T. Meshulam, V. Zakut, S. Spirex, A. Benderly, Z. Hochberg.

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Recent studies have shown that 1,25-D may be involved in the regulation of differentiation and function of the immune system. The syndrome of resistance to 1,25-D provides an opportunity for investigation of the role of 1,25-D in the immune system of human subjects. In this study we examined some aspects of the immune system in 5 patients with resistance to 1,25-D and alopecia who had defective receptors for 1,25-D in skin fibroblasts. All patients had normal numbers of blood T and B lymphocytes and normal helper/inducer (OKT4) to suppressor/cytotoxic (OKT8) ratio. Proliferative responses to phytohemagglutinin and concanavalin A were comparable to those of normal controls. Serum IgG, IgM and IgA were within the normal range for all patients. Staphylococcal killing and monocyte chemotaxis were comparable to controls in the one patient examined. Although phagocytosis of *Candida albicans* by neutrophils was normal, candidacidal activity was significantly lower ( $32 \pm 5\%$  of injected *C. albicans* in 1 hr) than that observed in the controls ( $83 \pm 16\%$  of injected *C. albicans* in 1 hr). The data indicate that 1,25-D participates in activation of intracellular killing of some microbes by human neutrophils and support the view that 1,25-D is involved in a wide range of cellular processes.

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# HUMAN THYMOCYTE CHEMILUMINESCENCE-DEPENDENCE ON MACROPHAGES. Senih M. Fikrig and Kamala Suntharalingam, Downstate Medical Center, Department of Pediatrics, Brooklyn, New York.

Rat thymocytes stimulated with Concanavalin-A (Con-A), in the presence of Luminol respond with a short lived burst of chemiluminescence (CL) associated with H<sub>2</sub>O<sub>2</sub> production. Macrophage depleted thymocytes are also said to react similarly.  $2.5 \times 10^7$  to  $1 \times 10^8$  thymocytes obtained from thymi resected during open heart surgery similarly responded to luminol augmented Con-A stimulation. Addition of latex particles further increased CL 5 to 10 folds. However partial elimination of macrophages by carbonyl-iron ingestion or by adherence to plastic surfaces reduced CL 5 to 7 fold from the initial values. Thymocyte CL may be a function of macrophages contaminating the cell suspension.

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# IMMUNE BASIS FOR EUSTACHIAN TUBE (ET) OBSTRUCTION Philip Fireman, Paul K. Stillwagon, David P. Skoner, Charles D. Bluestone, William J. Doyle (Spon. Thomas K. Oliver, Jr.) Children's Hospital, Pittsburgh, Pennsylvania

Recent studies in our laboratories have documented the development of allergic rhinitis (AR) and subsequent ET obstruction after provocative intranasal pollen or house dust mite antigen challenges in hypersensitive subjects. The induced ET obstruction was antigen dose dependent and inversely related to the patient's specific IgE antibody titer. Since prolonged ET obstruction underlies the pathogenesis of otitis media with effusion (OME), these data suggest a role for AR in the etiology of OME. To ascertain if ET obstruction and/or OME develop during natural pollen exposure, weekly bilateral ET function was measured by the 9-step pressure swallow tympanometric test. Eight children ages 5 to 14 years with documented ragweed AR and recurrent OME were studied before, during and after the 1984 ragweed season which was estimated by daily pollen counts. Ragweed allergy was confirmed by positive skin test with serum RAST ranging from 1 to 10 percent. Symptom score and medication diaries were kept. Whereas 9 of 16 ears (56%) showed normal ET function before pollen season and 10 of 16 (63%) after pollen season, only 2 of 15 (13%) had normal ET function at the peak of pollen season and 23 of 75 (30%) ears tested had normal ET function during the 5 week pollen season ( $p < 0.05$ ). OME did not develop in these patients. These studies have shown for the first time in children with a history of OME a causal relationship between an allergic reaction and the development of ET obstruction.

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# EVIDENCE FOR SECRETORY COMPONENT GENE EXPRESSION IN HUMAN LIVER. Randall M. Goldblum, Satya P. Kunapuli, Richard M. Denney, and Ashok Kumar.

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Polymeric immunoglobulin receptor (secretory component, SC) is an integral membrane protein synthesized by secretory epithelial cells and by hepatocytes of certain mammals. However, the synthesis, display and function of SC in human liver is not well characterized. We therefore sought evidence for SC synthesis by human liver using specific antibodies to SC and a library of phage expression vectors ( $\lambda$ gt11) containing cDNA copies of human liver messenger RNA.

In initial screening,  $3 \times 10^5$  phage were plated on E. coli (Y1090) and cultured for 3 hours before transfer to nitrocellulose filters containing the inducer IPTG. After 1.5 hr, the filters were probed using polyclonal antibody to SC and I<sup>125</sup> labeled protein-A. Clones positive by autoradiography were replated until all visible plaques gave positive signals for SC.

Primary screening of the library produced 6-8 discrete signals each time. Secondary and tertiary screens yielded progressive enrichment of SC-positive plaques. A mixture of 5 monoclonal antibodies to SC confirmed that tertiary clones produced an SC-like protein. While further studies will be necessary to confirm the specificity of the gene, our studies provide the first evidence that mRNA for SC is present in human liver. Although the cell of origin is undefined, the availability of cloned genes should allow us to further define the role of SC in this and other tissues.

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# CORRELATION OF FETAL OUTCOME WITH ANTENATAL TESTING IN ISOIMMUNIZED PATIENTS. Ronnie Guillet, Garrett Colmorgen, Soraya Abbasi, Chari Otis, Stuart Weiner.

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Sixty-seven pregnant women at risk for fetal isoimmunization were followed prospectively from 6/78-6/84 and scored by non-stress testing (NST) (reactive =2, nonreactive =0), amniotic fluid  $\Delta$  450 (slope: increasing =2, stable =1, decreasing =0), and fetal ultrasound (U/S) (erythroblastosis fetalis: none =2, minimal-moderate =1, moderate-severe =0). Postnatally, the 67 infants (GA  $36.6 \pm 3.1$  wks, mean  $\pm$  SD, BW  $2850 \pm 656$  grams) were independently scored without knowledge of the maternal score (living =2, dead =0; treatment: none =2, phototherapy =1, exchange transfusion =0; problems of prematurity: none =2, mild =1, moderate-severe =0). The mothers and infants were each assigned a rank from 1-10 according to their scores. A sign test (non-parametric) between the maternal and infant scores revealed no significant difference indicating agreement between rankings. The chi square goodness of fit for the distribution of scores when grouped as 1/2/3, 4/5/6/7, and 8/9/10 also indicated no significant differences in rankings. The correlation coefficient for infants rank against maternal rank was .76 at  $p < .001$ . No single antenatal test has thus far been shown to be predictive of neonatal outcome. We have shown prospectively that, in combination, NST,  $\Delta$  450 and U/S can reliably predict severity of isoimmunization. The composite score can therefore be used to optimize timing of delivery with respect to the risks of prematurity and erythroblastosis fetalis.

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# SECRETORY IGA ANTIBODIES IN HUMAN MILK AGAINST CANDIDA ALBICANS. Antony J. Ham Pong, Kimberly Hotko, Randall M. Goldblum, and Armand S. Goldman.

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Secretory IgA (SIgA) antibodies to *Candida albicans* have previously been detected in pooled human milk by immunofluorescence, and there is some evidence that these antibodies interfere with the adherence of that organism to human buccal epithelial cells (Arch Oral Biol 27:617, 1982). Little is known regarding the mucosal defense against this fungal agent in early infancy. Because of the occurrence of the fungus in the gastrointestinal tract, and the commonness of candidal infections during pregnancy, we hypothesized that high titers of SIgA antibodies to *Candida albicans* would be frequently present in human milk and would aid in the infant's mucosal defense against this fungus. Milk specimens, collected 2-4 days post-partum from 10 nursing mothers, were centrifuged to remove cells and examined for *Candida*-specific SIgA antibodies by a micromodification of an enzyme-linked immunosorbent assay, utilizing a protein extract of *Candida albicans* as the solid phase and an anti-secretory component-horseradish peroxidase conjugate as the detector. Pooled human colostrum served as a reference standard (titer 1:25). Eight of the subjects studied displayed titers of secretory IgA antibodies to *Candida* which were  $>1:16$ . The range of titers was  $<1:1$  to 1:460 (mean, 1:86; median, 1:32).

High titers of SIgA antibodies to *Candida albicans* found in the majority of milk specimens examined suggest that these antibodies may defend the mucosa of the breast-fed infant against this common opportunistic agent.